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EXAMINER

PORTNER, VIRGINIA ALLEN

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/607,834	Applicant(s) VOGEL ET AL.	
	Examiner GINNY PORTNER	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 June 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42, 85 and 86 is/are pending in the application.
- 4a) Of the above claim(s) 3, 5, 10-15, 26-42 and 85 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4, 6-9, 16-25 is/are rejected.
- 7) ☒ Claim(s) 86 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-42, 85-86 are pending.

Claims 1-2,4,6-9,16-25 are under consideration.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 28, 2008 has been entered.

Allowable Subject Matter

2. New Claim 86 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to Arguments

1. Applicant's arguments filed May 28, 2008 have been fully considered but they are not persuasive.

2. ***Rejections Maintained, Claim Rejections - 35 USC § 102:*** The rejection of claims 1-2,4,6-9,16-17,18, 19-21, 22-25 under 35 U.S.C. 102(b) as being anticipated by Pascual et al (WO97/18790) in light of evidence provided by Spevak et al 1996 incorporated by reference (particle attached carbohydrate) is traversed on the grounds that:

a. The combined teachings of Pascual reference and the Spevak reference describe the claimed invention.

3. In response to Applicant's statement that the prior art rejection is the "combined teachings of Pascual reference and the Spevak reference", it is the position of the examiner that Pascual et al inherently anticipates the instantly claimed invention in light of Spevak, a reference incorporated by reference into Pascual,. The prior art rejection is an inherency rejection.

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EXAMPLE 14

FAM screening matrices. Matrices displaying physiological ligands for PAMs are prepared from known carbohydrate and glycoprotein counter-receptors that bind cellular receptors used by pathogenic microbes. Various macromolecular structures have been designed by the inventors for use as diagnostic materials for the rapid screening of pathogens for PAMs. For developing carbohydrate-terminated matrices, the inventors use a method (Method 1) described by Spevak et al (Spevak, W., et al. 1996, J. Med. Chem. 39:1018-1020) for the construction of acidic multivalent assemblies displaying carbohydrate ligands for detecting or identifying PAMs in the shear assay system. These matrices consist of an acidic lipid scaffolding supporting glycolipid ligands that are used to coat the internal walls of capillary

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tubes. Carbohydrate-terminated lipid matrices are made stable by polymerization with UV. Another Method (Method 2) consists of diluting the N-glycosides or glycolipid in methanol, drawing approximately 100ul containing 100 ng glycolipid into a capillary tube and allowing the solvent to evaporate overnight at 37°C. The lumen of the tubes is then coated with 200ul of 2% bovine serum albumin (BSA) in phosphate buffered saline (PBS) for 2 hours, washed twice with the BSA solution, and finally flushed free of the coating solution. For developing glycoprotein-terminated matrices, a Method 3 includes incubation of glycoprotein adhesion molecule constructs in HBSS media (100ug/ml) containing Ca++ and Mg++ plus detergent for one hour at 37°C in capillary tubes. The tube is then cooled to 4°C for 15 minutes and flushed (washed) with HBSS medium maintained at 4°C. The inventors have developed an extensive panel of purified glycoproteins including E- and P-selectins, ICAM, VCAM, MadCAM-1 and β 1 and β 2 integrins. Using Methods 1, 2 or 3, the inventors have formulated several novel FAM screening matrices for use as diagnostic reagents in the shear assay system. These include but are not limited to the following.

Instant claims 1-2: The above narrative taken from Pascual et al teaches a shear assay system (see Pascual et al, claim 52). The assay combines the pathogen's adhesion, which is called I-FABSDAM in Applicant's claims, together with host target cell expressing the ligand for the adhesion, or with purified ligands for the target cell (see Pascual et al, claims 51-52, page 91), the ligand is called FAMSDB-L in Applicant's claims. Therefore Pascual et al combine an adhesion molecule and its ligand to bring about binding, and then add shear stress under flow conditions to change the bond stress between the two molecules (see Pascual et al, claim 52; see page 71 for table of adhesins and carbohydrate ligands). One type of pathogen adhesion

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disclosed includes a peptide domain of the adhesive lectin region on fimbriae displayed by *Escherichia coli* and *Salmonella typhi* (see Pascual, page 87, claims 21 and 30) which is combined with a carbohydrate ligand (mannose, see Pascual claims 15-16; see page 72, lines 1-18) present on endothelial cells or in purified form (see Pascual claim 15, page 85).

4. Applicant states that Pascual et al does not disclose "after the binding, changing a bond stress on the I-FABSDAM.

5. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., after binding changing a bond stress) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

6. Additionally, Pascual et al disclose flow shear force bond stress changes between an adhesin under static conditions and then under shear bond stress conditions wherein the bond strength increases with increase shear stress (see Pascual et al, page 16, Table 1). Clearly the data presented in Table 1, shows an increase in bond stress under shear forces, as well as a decrease in bond stress under shear based upon the evident changes induced by Shear forces for **E-selectin, P-selectin, and L-selectin**.

15 Table 1
Adhesion Molecules Examined Under Shear
Adhesion Molecule Expressed on Optimal
Function Conditions

	Leukocyte	Endothelium	Shear	Static
20 E-selectin	-	+	+	-
P-selectin	-	+	+	+
L-selectin	+	+	+	-
MAACAM-1	-	+	+	+
PNAd	+	+	+	+
VCAM-1	+	+	+/-	+
25 ICAM-1	+	+	-/+	+
Mac-1	+	+	-	+
1-LFA-1	+	-	-	+
VLA4	+	-	-	+
beta -1	+	+	-/+	+
30 LPAM	+	-	-/+	+

7. This same Shear Force assay format is disclosed for microbial adhesins (see page 17, lines 16-21) and their ligands. Clearly Pascual disclose the instantly claimed invention as now claimed.

Therefore, in light of Applicant's definitions of the terms recited in the instant claims, Pascual et al still anticipates the instantly claimed invention because Pascual et al disclose molecules that are adhesins (selectins) binding to ligands on the surfaces of cell membranes. Instant claim 1 is not limited to a method of evaluating bacterial adhesins bond strength but encompasses eukaryotic adhesins in association with cell membrane associated ligands, the bonds of which are changed due to shear stress. While Pascual evaluates competitive inhibitors of known adhesion/ligand binding strength under **shear forces**, these competitive inhibitors meet the definition provided in Applicant's specification which defines the adhesion molecule to be "FABSDAM" refer to **molecules that are capable of binding ligands in a force-activated bond stress-dependent manner.**" The method of Pascual et al still anticipates the instantly claimed invention as now claimed.

Original prior art rejection: Pascual et al disclose the instantly claimed method, the method comprising the step (see page 12, lines 15-33; page 30, lines 33-36 "an in vitro shear assay system"; "Assessment of the adhesivity of pathogens with target cell receptors under different levels of shear force (see page 31, lines 10-19)", see page 41 of :

Instant claim 1, 22, 25: Changing a bond stress of an isolated force activated bond stress dependent adhesion molecule (see page 60 line 17 "purified"; page 64, lines 21-22 "purified adhesion of adhesion-positive microbes"; page 16, Table 1, and lines 6-7 "in vitro assays under high shear conditions designed to reflect blood flow"; E-selectin; P-selectin; L-selectin binding to ligands on endothelium or leukocytes, wherein binding increases in the presence of shear force (shear, positive binding) and decreases in the absence of shear forces ("static" and negative binding).

to a force activated bond stress dependent binding ligand; protein-carbohydrate interactions (see page 13, lines 9-10) ; "different glycoconjugates that function as counter-receptors for pathogen adhesion molecules" (page 19, lines 31-32); also see page 32, lines 18-27 "adhesion molecule of a pathogenic organism which interacts with receptor molecules of a cell); "multivalent assemblies displaying carbohydrate ligands (page 59, lines 31-32).

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Instant claim 2: wherein the bond stress is shear force (see page 16, Table 1, and lines 6-7 “in vitro assays under high shear conditions designed to reflect blood flow”;

Instant claim 4: binding increases in the presence of shear force (shear, positive binding) and decreases in the absence of shear forces (“static” and negative binding). (see page 16, Table).

Instant claim 6: wherein the method results in tightly bound adhesion and ligand binding (See page 17 “shear-dependent attachment and rolling”.; “activation dependent adhesion strengthening (slowed rolling), followed by tight adhesion”).

Instant claim 7: wherein the adhesion molecule is microbial lectins (see page 17, lines 16-30), or an adhesin, selectin, integrin, immunoglobulin superfamily cell adhesion molecule or microbial lectin

Instant claim 8: wherein the adhesion comprises polypeptide (see claim 30, “the adhesive lectin region on fimbriae displayed on microbes selected from the group consisting of Escherichia coli, Neisseria gonorrhoeae, Neisseria meningitides, Salmonella typhi, Salmonella typhimurium, Pseudomonas aeruginosa and Yersinia enterocolitica, page 87 and page 71, Salmonella typhi and typhimurium, fimbrial adhesion binds to mannose, and is therefore a FimH polypeptide. polypeptide). “Lectins frequently appear on the surface of the cell, on specific organelles, such as bacterial fimbriae or are part of the structure of exotoxins elaborated by bacteria.”

Instant claim 9: wherein the FimH polypeptide is an E.coli FimH polypeptide (see page 71, E.coli binding to mannose, and therefore is a FimH, E.coli polypeptide). While the reference does not mention the term “FimH”, in light of evidence provided by Swiss-Prot accession numbers P08191 and Q9R5Y2 that show both E.coli and Salmonella to express a polypeptide that binds to mannose and is referred to as FimH.

Instant claim 16-17: mannose or oligomannose (see mono or oligosaccharide, both simple or complex (page 11, lines 35-36; and page 71, carbohydrate specificity column “Mannose”). see page 11, lines 35-36 and page 12, lines 1-7 “Lectins bind reversibly and noncovalently with mono or oligosaccharides, both simple and complex” and page 72, lines 16-17).

Instant claim 18: wherein the adhesion molecule is attached to a particle, the particle being a bacterial pili (also known as Fimbrial adhesion, see page 71) being “bead-bound”(see page 41, lines 16-17); see “E.coli coated beads (see page 44, line 40), or “purified glycoproteins” that are incorporated into screening matrices (see page 60, lines 16-22 and page 61) thus producing a synthetic molecule associated with a synthetic substrate surface.

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Instant claim 19: wherein the ligand is attached to a particle (see page 59, Example 14 “carbohydrate terminated matrices” in light of Spevak et al, 1996, incorporated by reference) purified ligand coated on the luminal surface of a capillary tube reaction chamber” see page 56, lines 28-31)

Instant claim 20-21: ligand attached to a particle, the particle being a synthetic molecule (in light of teaching by Spevak et al incorporated by reference, particles), or coated on a device surface which is a synthetic substrate surface.

Instant claims 23-25: wherein changing said bond stress comprises applying a bond stress within the claimed ranges of 1-3 dynes/cm² (see page 41, line 8).

Pascual et al anticipates the instantly claimed invention directed to a method that increases bond strength by of a bacterial lectin adhesins present in purified fimbria of Salmonella and E.coli that bind to mannose or oligomannose ligands each of which are attached to a particle, in light of Spevak (1996, incorporated into Pascual et al by reference, page 59, lines 29-30) that teach particles for attaching carbohydrate ligands.

1. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594
2. Inherently the reference anticipates the now claimed invention. *Atlas Powder Co. v IRECA*, 51 USPQ2d 1943, (FED Cir. 1999) states AArtisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

1. The rejection of claims 1-2,4,6-9,16-17,18, 19-21, 22-25 under 35 U.S.C. 102(e) as being anticipated by Bargatze et al, (US PG Pub. 2004/0247611, effective filing date November 23, 1998) is traversed on the grounds that:

- a. Bargatze et al does not describe every element of the claimed invention, specifically the reference “fails to disclose an isolated force activated stress dependent adhesion molecule (I-FABSDAM) or a force activated bond stress dependent binding

ligand (FABSDB-L)” and concludes that “the cited reference does not exactly describe the invention as now claimed” and states the claimed invention requires the IFABSDAM to not be in “the same context in which they exist in nature

b. Bargatze shows an assay that evaluates the interaction between the pathogen adhesion molecule and its corresponding ligand to identify a pathogen.

2. Bargatze discloses a method of “identifying pathogen-ligand interactions under shear conditions (abstract)”, the interactions being those associated with an in vitro blood vessel shear flow system [0018], also see claim 66 “carbohydrate” claim 65 “ligands coated on beads”, and produce differing types of physiological shear stress (see claim 59) .

3. Bargatze disclose the utilization of adhesins that are not in the native location (see claims 70, 78 and 80, “isolated pathogen adhesion molecules”) , but are isolated: [0223] The isolation of a pathogen's adhesion (attachment) molecule (PAM) which mimics that expressed on host cells begins with its detection and characterization in the inventors in vitro shear assay system using target cells that express the ligand for the adhesion molecule or purified ligands coated on the luminal surface of a capillary tube reaction chamber.

4. Bargatze goes on to describe binding after application of shear assay bond stress: [0230] PAM screening matrices.--Matrices displaying physiological ligands for PAMs are prepared from known carbohydrate and glycoprotein counter-receptors that bind cellular receptors used by pathogenic microbes. Various macromolecular structures have been designed by the inventors for use as diagnostic materials for the rapid screening of pathogens for PAMs. For developing carbohydrate-terminated matrices, the inventors use a method (Method 1) described by Spevak et al (Spevak, W., et al. 1996. J. Med. Chem. 39:1018-1020) for the construction of acidic

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multivalent assemblies displaying carbohydrate ligands for detecting or identifying PAMs in the shear assay system. These matrices consist of an acidic lipid scaffolding supporting glycolipid ligands that are used to coat the internal walls of capillary tubes. Carbohydrate-terminated lipid matrices are made stable by polymerization with UV. Another Method (Method 2) consists of diluting the N-glycosides or glycolipid in methanol, drawing approximately 100 .mu.l containing 100 ng glycolipid into a capillary tube and allowing the solvent to evaporate overnight at 37.degree. C. The lumen of the tubes is then coated with 200 .mu.l of 2% bovine serum albumin (BSA) in phosphate buffered saline (PBS) for 2 hours, washed twice with the BSA solution, and finally flushed free of the coating solution. For developing glycoprotein-terminated matrices, a Method 3 includes incubation of glycoprotein adhesion molecule constructs in HBSS media (100 .mu.g/ml) containing Ca^{++} and Mg^{++} plus detergent for one hour at 37.degree. C. in capillary tubes. The tube is then cooled to 4.degree. C. for 15 minutes and flushed (washed) with HBSS medium maintained at 4.degree. C. The inventors have developed an extensive panel of purified glycoproteins including E-L- and P-selectins, ICAM, VCAM, MAdCAM-1 and .beta.1 and .beta.2 integrins. Using Methods 1, 2 or 3, the inventors have formulated several novel PAM screening matrices for use as diagnostic reagents in the shear assay system.”

5. It is the position of the examiner that the terms (I-FABSDAM) and (FABSDB-L) are terms that are defined in the Specification to represent a genus of molecules with specific functional characteristics; the functional characteristics being adhesion activity and adhesion binding activity, respectively. The instant method requires the (I-FABSDAM) and the (FABSDB-L) to bind to each other and for the bond stress to be changed, the change including

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increased binding strength under shear flow conditions. One mode of increasing bond stress defined, as defined in the instant Specification, is flow bond stress induced changes.

Prior art rejection: Bargatze et al disclose and claim a method of increasing the bond strength of an adhesion molecule (see page 25, claims 55-56 “soluble pathogen adhesins” introduced to a moving fluid that creates shear flow conditions), wherein the adhesins are contacted with carbohydrate ligands coated on beads (see page 25, claims 65-66 “carbohydrate”), the method comprising the step of :

binding the adhesion with the ligand :

“(55. A method for identifying pathogen-ligand adhesive interactions under shear flow conditions, wherein the ligand is immobilized on a substrate.

56. The method of claim 55 comprising: (a) coating the surface of said substrate with a candidate ligand or target cells expressing a candidate ligand; (b) moving a fluid across the substrate to create shear flow conditions; (c) introducing pathogens or soluble pathogen adhesins into said moving fluid; and (d) observing adhesive interactions between said pathogens and said coated substrate under shear flow conditions to identify pathogen-ligand adhesive interactions” and

changing the bond stress of the isolated adhesion so that the bond stress increases under shear force flow conditions (see claims 55-56 and Table 1, page 5; Example 14, page 17, and table on page 17-18; Example 16; tables on page 20-21, especially the Microbial Pathogen carbohydrate binding protein that bind to carbohydrate ligand.)

Bargatze et al still anticipates the instantly claimed invention as now claimed as the claimed methods steps may be carried out in any order “comprising”, as well as carried out in the

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claimed order, as Bargatze et al evaluate the bond strength under shear flow stress conditions between an adhesion and ligand which are bound to each other.

3. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594
4. Inherently the reference anticipates the now claimed invention. *Atlas Powder Co. V IRECA*, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. AThe Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.
6. The rejection of claims 1-2, 4, 6-7 under 35 U.S.C. 102(b) as being anticipated by Brooks et al (1983) is traversed on the grounds that:

- c. The reference does not disclose an isolated force activated stress dependent adhesion molecule or a force activated stress dependent binding ligand as required by the claims.

7. It is the position of the examiner that claimed method encompasses isolated organisms (see claim 18), and Brooks isolated *Aeromonas salmonicida* strain 438, which is a bacterial organism. *Aeromonas salmonicida* strain 438 comprises the adhesion, and contacted the isolated adhesion with its ligand attached to a particle, specifically erythrocytes under shear stress.

Applicant's definition of I-FASDAM includes " [0111] In the practice of this invention, a FABSDAM or an isolated FABSDAM (I-FABSDAM) and/or a FASBSDB-L can be attached to a particle, including, but not limited to bacterial pili, naturally occurring isolated molecules,

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synthetic molecules, proteins, polypeptides, organelles, prokaryotic cells to which said FABSDAM is not native, eukaryotic cells to which said I-FABSDAM is not native, viruses, organisms, nanoparticles, microbeads, and microparticles or to a surface selected from the group consisting of cell membranes, other biological membranes, device surfaces and synthetic substrate surfaces.”

Brooks et al still anticipates the instantly claimed invention as now claimed.

Original Prior art rejection: Brooks et al disclose the instantly claimed invention directed to a method comprising the step of increasing the bond strength (see page 320, paragraph 2, last full sentence; page 321, paragraph 1 “This second phase represents a marked strengthening of the aggregation and hence of bacterial adhesion induced by shear in the system”) of an isolated adhesion of E.coli pili, wherein the increase in bond strength was induced by shear force (see page 327, Figure 10 and page 328, Figure 11), and wherein the ligand was A+ human erythrocytes that are known to present D-mannose/L-fucose carbohydrate ligand (see figure 2, ledger, line 3 and Figure 2 alphaMM defined at page 321, paragraph 2, line 5). Brooks et al anticipates the instantly claimed invention as now claimed.

Conclusion

1. This is a non-final action.
8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Various references have been cited to show shear force stress assays, microbial adhesins or adhesions to cell receptors. See Shvets et al, (US Pat. 7,122,301, claim 1, flow shear stress assay claimed).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Shanon Foley or Robert Mondesi, can be reached on 571-272-0898 and 571-272-0956, respectively. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Ginny Portner/
Examiner, Art Unit 1645
August 12, 2008

/Mark Navarro/
Primary Examiner, Art Unit 1645